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SIM & MCBURNEY
330 UNIVERSITY AVENUE
6TH FLOOR
TORONTO, ON M5G 1R7
CANADA

EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	PAPER NUMBER
1648	

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14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/577,601	LOOSMORE ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 1-13 are pending and under consideration in this application.

2. Because this application raises new rejections not raised in the action mailed on June 6, 2002 (the prior action), and not necessitated by an amendment to the claims, the Office Action is being made Non-Final.

Information Disclosure Statement

3. The IDS filed on December 4, 2002 has been considered, and a copy of the signed paper is attached to this Action.

Drawings

4. New corrected drawings are required in this application for the reasons indicated on the attached form PTO 948. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Double Patenting

5. **(Prior Rejection-Maintained)** Claims 1-3 were rejected in the prior action under the judicially created doctrine of obviousness-type double patenting as being unpatentable over

claims 7 and 11 of U.S. Patent No. 5,506,139. The applicant traverses this rejection on two grounds. First, the applicant argues that the prior patent is silent about, and does not teach the inclusion of the leader sequence in the claimed nucleic acid. This argument is not found persuasive. As the examiner pointed out in the prior action, the portions of the specification supporting the claims of the prior patent disclose the gene encoding the Hin47 protein, including the leader sequence. While the application is silent regarding the inclusion of the leader sequence in the isolated nucleic acid, claim 7 of the application recites a nucleic acid "comprising a mutant Haemophilus influenzae hin47 gene" coding for a Hin47 analog. From this, one of ordinary skill in the art would assume that that claimed nucleic acid includes the entire Hin47 gene, including the leader sequence, and the modifications required elsewhere in the claim.

The second argument in traversal of the double patenting rejection is based on an argument that the prior patent does not teach an expression vector. The applicant is not convinced that a claim to the nucleic acid does not render obvious an expression vector comprising that nucleic acid. However, even if such were the case, the rejection would be maintained on the basis of claims 14 and 15 of the prior patent, which describe a "recombinant plasmid adapted for transformation of a host cell," and a specific plasmid. Such a plasmid would be, and include an expression vector encoding the Hin47 analog. See e.g., column 14, lines 42-46 (describing the cloning of a Hin47 analog into an expression vector to make such a plasmid). In view of these teachings by the prior patent of the claimed invention, the examiner finds that it would have been obvious to one of ordinary skill in the art to make an expression vector from the claimed nucleic acid.

6. **(New Rejections)** Claims 1-3 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 7-12 of U.S. Patent No. 6,147,057; claims 1-12 of U.S. Patent No. 6,025,342; claim1-12 of U.S. Patent No. 5,981,503; claims 10, and 12-20 of U.S. Patent No. 5,939,297; and claims 11, and 13-22 of U.S. Patent No. 5,869,302. Although the conflicting claims are not identical, they are not patentably distinct from each other for substantially the same reasons as stated above with reference to claims 7 and 11 of U.S. Patent No. 5,506,139.

More particularly, with reference to the immunogenic compositions claimed in patents 6,147,057, 6,025,342, and 5,981,503, the immunogenic compositions are disclosed in the abstracts of these patents as producing the Hin47 protein, or protein capable of eliciting anti-Hin47 antibodies, in a host cell. The claims of patents 5,939,297 and 5,869,302 teach a recombinant plasmid containing a nucleic acid encoding for the Hin47 analog, and the abstracts of the patents teach the use of the plasmids to produce the analog in a host cell. Thus, the claims and portions of the application discussing the claimed products, of these patents teach or suggest the presently claimed expression vectors.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Specification

8. **(Prior Objection-Withdrawn)** The disclosure was objected to in the prior action because of the following informalities: the specification refers to patent application number 09/268,347. pp. 3, line 18; 12, line 12, p16, line 31. This application is now patented, patent number 6,335,182. In view of the amendments made to the application, the objection is withdrawn.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. **(New Rejection-Necessitated by Amendment)** Claims 4, 12, and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As amended, the claims are limited in scope to specific plasmids encoding a Hin47 analog. These claims are rejected as the applicant has not enabled one of ordinary skill in the art to make or use these exact plasmids. In the specification of the application, the applicant has provided a description of how the applicant

made the claimed plasmids. However, the applicant did not describe the claimed plasmids, or the plasmids from which they were derived, in adequate detail such that one of ordinary skill in the art would be able to replicate the applicant's invention as claimed. For example, the applicant did not state where the plasmids used to make the claimed plasmids may be obtained, or all of the characteristics (e.g. sequence) of either these plasmids, or the plasmids actually claimed. Absent such information, one skilled in the art would not be able to make or use the claimed plasmids.

In order to fully enable these claims, the applicant must make a biological deposit of the claimed plasmids.

11. **(New Rejection-Necessitated by Amendment)** Claims 4, 12, and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims have been described above. The claims are rejected for lack of written description because the applicant has not provided sufficient disclosure in the application to allow one in the art to make or use the claimed plasmids. The applicant has not stated where one skilled in the art could acquire the plasmids used to make the claimed plasmids, nor the information (sequence) of either the claimed or used plasmids such that one skilled in the art would know which plasmids are being claimed by the applicant or used to make the claimed plasmids.

12. **(Prior Rejection- Maintained)** Claims 1 and 5, and dependant claims 6, 9-11, and 14 were rejected in the prior action under 35 U.S.C. 112, first paragraph, because the specification,

while being enabling for an expression vector encoding a non-proteolytic analog created by the substitution or deletion of one or more of amino acid residues 91, 121, and 197, does not reasonably provide enablement for any non-proteolytic Hin47 analog. The applicant traverses this rejection on the grounds that 1) one of ordinary skill in the art would be able to develop non-proteolytic analogs using methods that are routine in the art and 2) that the applicant has been issued a claim akin to the rejected claim in scope (i.e. covering any non-proteolytic analog).

These arguments are not found persuasive by the examiner. With regards to the first argument, the Examiner agrees that one of ordinary skill in the art may be able to develop non-proteolytic analogs using the routine methods known in the art. However, the applicant has set no limit on what may comprise an analog of the Hin47 protein. See e.g., App., page 4, line 31-page 5, line 4 (stating that an analog "may" comprise one of the claimed substitutions). While the applicant has said what an analog will not do (non-proteolytic), the applicant has not said what the analog will do. A person skilled in the art could create a mutant of the Hin47 protein by deleting a majority of the residues it comprises. In such a case, the protein may lose not only its protease activity, but also any other value it has as an immunogen or a chaperone protein (the other disclosed uses for the Hin47 protein). See e.g., App. page 2, lines 17-22. One practicing the invention would, in that case, be left with a protein with no utility. In other words, the applicant has not provided sufficient information in the disclosure to allow one skilled in the art to use *any* non-proteolytic analog of the Hin47 protein, because the applicant has not shown how to use analogs with neither of the other utilities suggested by the application.

Just as the applicant has not disclosed a use for any non-proteolytic analog of the Hin47 protein, the applicant has also provided insufficient guidance to allow one skilled in the art to

make or use any other analog that is either immunogenic or useful as a chaperone. This is because the applicant has not indicated what regions of the protein, or individual resides, are necessary for either of these functions, other than the substitution of one of the residues 91, 121, or 197. Outside of mutation of these residues, the applicant has not shown that any other analog will have any of the utilities discloses in the application. However, with over 200 residues available for substitution, not to mention the potential for additions and deletions, the range of analogs according to the claims is great. Again, however, the applicant has not provided any guidance as to which of these numerous mutations will leave those in the art with a useful Hin47 analog.

The applicant has described in the present application what amino residues are necessary for either the immunogenicity of the Hin47 protein, or its ability to act as a chaperone. Without such guidance, it would be left to those desiring to practice the claimed invention to determine for themselves what modifications may be made to the Hin47 protein to make a useful non-proteolytic analog. As was pointed out above, there are a large number of potential mutations that may be made to the Hin47 protein. There is also, in the present application, a dearth of guidance from the applicant as to which of these mutations would be operative. One skilled in the art would not know from the present application what effects a mutation at any residue other than at positions 91, 121, and 197 would have. Given all of these factors, and the generally accepted unpredictability in the art of protein modification (see e.g. Bowie et al., Science Vol. 247:1306-1310), the examiner finds that the applicant has not provided sufficient disclosure to enable one skilled in the art to practice the present invention to the full scope of the claims without undue experimentation.

The examiner must respectfully decline to withdraw the rejection for the reason that the applicant has been issued claims similar to the rejected claims in a prior application with a similar disclosure. While the applicants' argument has some weight, the examiner does not find it sufficient to overcome the rationale supporting the present rejection. As the applicant has not provided any reason other than the issuance of the prior patent as to why the rejection should be withdrawn, the rejection is maintained for the reasons of record, and for those reasons discussed above.

13. **(Prior Rejection-Maintained)** Claims 1, 2, 5, 6, and 7 were rejected in the prior action under 35 U.S.C. 112, first paragraph. The specification, while being enabling for a non-proteolytic Hin47 analog wherein the analog includes a substitution or deletion of at least one of the amino acid residues 91, 121, or 197, does not reasonably provide enablement for the analog with the substitution or deletion of amino acids 195, 196, or 198-201. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. This is because the applicant has not shown that the substitution or deletion of any of amino acids 195, 196, or 198-201 would create a non-proteolytic analog.

The applicant traverses this rejection on the basis that the "there is no reason to suppose that mutation of [residues 195, 196, or 198-201] would not result in loss of proteolytic activity." The examiner disagrees. As the applicant pointes out, column 5 of the related patent 5,506,139 refers to a consensus sequence of the active site of serine proteases. The consensus sequence of the proteases varies from the sequence in 3 of the 7 residues in the 198-201 residue sequence. As

the consensus sequences is presumed to be derived from the varying sequences of *active* proteases, it would appear that other active serine proteases contain variations in their counterparts of the disclosed region that do not inhibit the activity of the proteins. It would therefore seem apparent that the disclosed sequence is amenable to residue substitutions within the described range. Thus, there is evidence that not every substitution in this range would result in the loss of proteolytic activity. Thus, the applicant's argument that "there is no reason to suppose that mutation at such sites would not result in the loss of protease activity" is itself an unsupported argument. As the applicant has provided no more than unsupported argument in traversal of the rejection, and as the examiner has shown reason to expect that modifications of such other residues would not result in loss of protease activity, the rejection is maintained.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. **(Prior Rejection- Withdrawn)** Claims 4, 12, and 13 were rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims includes the language "a plasmid vector having the *identifying characteristics of* plasmid..." (italics added). The claims as amended no longer include this language. The rejection is therefore withdrawn.

16. **(New Rejection Necessitated by Amendment)** Claims 4, 12, and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The applicant has

not identified either the claimed plasmids, or those plasmids used to construct them, to such an extent that one skilled in the art could recognize what is being claimed. Absent a source of the plasmids, or a sequence of the entire plasmid, from which one skilled in the art could compare other plasmids, such a person would not know whether or no they were in possession of one of the claimed plasmids.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. **(New Rejection)** Claims 1-3 are rejected as anticipated under 35 U.S.C. 102(b), or in the alternative, as rendered obvious under 35 U.S.C. 103(a), by U.S. Patent 5,506,139. The claims of the application at issue describe an expression vector encoding for a non-proteolytic analog of Hin47, its leader sequence, and a promoter, wherein said analog is a mutation of the natural protein in which at least one of the following residues has been substituted or deleted: residues 91, 121, and 195-201. The patent teaches a nucleic acid according to the claims, but does not explicitly describe the nucleic acid as containing either the leader sequence or the promoter of the gene, or as an expression vector. However, the patent does teach the making of recombinant plasmids for the use in transforming cells that include the claimed nucleic acid, and teaches including the nucleic acid is in an expression vector for its inclusion in a plasmid. Col. 114, lines

42-46. Further, the patent also claims that the nucleic acid included in the claimed plasmids are mutant Hin47 genes. Claim 7. As the patent discloses the Hin47 gene, including the leader sequence, the reference either anticipates, or renders obvious, the claimed expression vector.

19. **(Prior Rejection-Withdrawn)** Claims 1-3 were rejected in the prior action under 35 U.S.C. 102(b) as being anticipated by the 1998 Infection and Immunology article "The Haemophilus Influenzae HtrA Protein Is a Protective Antigen " (the 1998 article) by Loosmore et al. The applicant traversed the rejection on the grounds that the reference does not teach the creation of an expression vector encoding a non-proteolytic analog of the HtrA protein. The examiner agrees with the applicant that it appears that the reference teaches expression vectors not including the leader sequence, and non-expression vector nucleotides encoding the HtrA wild-type gene. As the examiner found the applicant's arguments persuasive, the anticipation rejection is withdrawn.

(Prior Rejection-Withdrawn) Claim 4 was rejected in the prior action under 35 U.S.C. 102(b) as being anticipated by the 139 patent. Claim 4 describes a plasmid vector "having the identifying characteristics of plasmid JB-3120-2 as seen in Figure 1A." The claim has been amended so that it reads on the precise plasmid identified in the claim. As the reference does not teach this plasmid, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. **(Prior Rejection-Withdrawn)** Claim 4 was rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over the 139 patent in light of U.S. Patent Number 6,361,969, issued to Galeotti (the Galeotti patent) and Recombinant DNA, 2d edition, by Watson et al. In view of the amendment to this claim, and the fact that the precise plasmid claimed by the applicant is not taught or suggested by the prior art, the rejection is withdrawn.

22. **(Prior Rejection-Maintained)** Claims 5-8 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Bass et al, J. Bacteriology (Bass), 178:1154-61, in view of the 1998 article (above), and U.S. Patent number 5,474,914, issued to Richard Spaete (the Spaete patent). These claims describe an expression vector comprising DNA encoding a non-proteolytic analog of Hin47, an additional protein, and a regulatory element. Claim 6 further requires that the vector also encode a Hin47 leader sequence. Claims 7 and 8 further limit the vector to one in which the Hin47 analog is a substitution or deletion mutant of one of the residues 91, 121, or 195-201 of the natural Hin47 sequence.

The applicant traversed this rejection with the following arguments: 1) that Bass does not teach that an non-proteolytic analog could function as a chaperone protein, 2) that Spaete does not teach the use of the Hin47 as a chaperone, and 3) that the 1998 article does not teach an expression vector encoding a non-proteolytic analog of Hin47 including the leader sequence. The

applicant does not find the applicant's arguments persuasive. Each of these arguments targets a single reference used in the rejection. They do not address what is taught by the references cumulatively.

The first argument forwarded by the applicant in traversal of this rejection argues that Bass does not teach that the Hin47 protein could act as a chaperone when the protein has lost its proteolytic activity. The examiner is not persuaded by this argument because the reference teaches, "the proteolytic efficiency of the complex would thus decide the fate of the protein." Bass, page 1157. From these teachings, the reference indicates that the proteolytic activity is not essential to the proteins activity as a chaperone. In actuality, the more effective the protease activity of the protein, the less effective it is as a chaperone. As the reference indicates that the protease activity of the Hin47 inhibits its value as a chaperone, and as the reference does not provide any reason to suspect that this activity is necessary to the proteins secretion from a cell, one of ordinary skill in the art would have had a reasonable expectation that a mutant Hin47 not expressing this proteolytic activity would be a more effective chaperone than the native protein. It is noted that those in the art need only a reasonable expectation of success, not a certainty. The applicant has not provided any evidence that as to why one of ordinary skill in the art should not have had such an expectation. In view of the teachings of Bass teaching that the proteolytic activity is a limiting, not a positive, factor in the use of the Hin47 as chaperone, the examiner is not persuaded by this traversal.

The applicant next argues the insufficiency of the 1998 article. It is noted that the examiner agrees with the insufficiency of this article as a 102 reference. The examiner also agrees that, alone, the reference alone appears to provide no motivation to make an expression

vector including the leader sequence. However, when combined with the teachings of Bass, and knowledge of those in the art of the importance of the leader sequence in achieving protein secretion, the examiner finds that one of ordinary skill in the art would then have had a motivation to include the leader sequence in the expression vectors described by the reference.

Finally, the applicant also argues that Spaete is neither enabling for any combination of desired protein and compatible escort, and that Spaete does not specifically teach the use of Hin47 as such an escort. However, Spaete is not used by examiner to teach or enable the practice of the claimed invention. Spaete's relevance is limited to the 1) inclusion of the desired protein and the chaperone in the same vector, and 2) the necessity of the inclusion of a leader sequence in the chaperone. Thus, while the examiner agrees that Spaete reference alone may not enable one of ordinary skill in the art to practice the presently claimed invention, the examiner does not find this to be dispositive of its value as an obviousness reference when combined with the other references cited above. First, when Bass and Spaete are read in light of each other it would clearly be obvious to one of ordinary skill in the art that Hin47 is a potential chaperone. Further, when the 1998 article is also read, it would be clear from the combination of this article with Bass that the non-proteolytic Hin47 would be of greater value than the native form with an uninhibited protease activity. Finally, in view of the teaching of Spaete indicating that the leader sequence is important to the efficacy of the chaperone, it would have been obvious to those in the art to construct the vectors taught by the 1998 article such that they include these sequences. While Spaete indicates that non-homologous leader sequences may be used (note that the teaching of such in column 21 of the patent is an alternative), it would be obvious to those in the art to make Hin47 chaperones with the native sequence both for convenience, and because it can

fairly be assumed that this sequence would be effective in allowing the secretion of the Hin47 analog. For these reasons, and for the reasons of record, the examiner maintains the stated rejection.

23. **(Prior Rejection- Maintained)** Claims 9-11 were rejected under 35 U.S.C. 103(a) as being unpatentable over Bass, in view of the 1998 article, and the Spaete patent, and further in view of Barenkamp and St. Geme III, Molecular Microbiology 19:1215-23 (Barenkamp), and U.S. Patent Number 6,335,182 (the 182 patent). These claims describe a an expression vector encoding a non-proteolytic Hin47 analog, a regulatory element, and an additional nucleic acid molecule encoding for another recombinant protein, wherein that recombinant protein is the Haemophilus influenzae Hia protein.

The applicant traversed this rejection on the grounds that 1) the combination of the 1198 article, Spaete, and Bass does not teach the vector of claim 5, and 2) that the additional references do not teach or suggest the combination of the Hia protein in the vector of claim 5, or even suggest a multiantigen vaccine combining the Hin47 protein with the Hia protein. The first argument has been adequately addressed in the response to the traversal regarding claim 5 above.

In response to the applicant second argument, the examiner would first like to draw the applicant's attention the U.S. Court of Customs and Patent Appeals case In re Kerkoven. 205 U.S.P.Q. 1069. This case states in no unclear terms that "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose." Id., at 1072. In view of this, and the fact that both the Hin47 and the Hia proteins were known antigens to

Hemophilus influenzae, it would have been obvious to make an antigenic composition comprising both of these proteins.

Further, one of ordinary skill in the art would also have known from the references that the non-proteolytic analog of the protein both retains its immunogenicity (1998 article, page 902) and may be used as a chaperone (as described above). Such person would also have been motivated to make a single vector that expresses both these proteins, as doing so would be a more efficient way of producing the combined composition. In view of this, it would likewise have been obvious to such a person to make use of the Hin47 analog's utility as a chaperone protein in the production of the combined Hin47 and Hia antigenic composition. Thus, there is motivation for the creation of the claimed vector. There would also have been a reasonable expectation of success in the combination as the combination is merely making use of known properties of the constituent proteins.

For these reasons, and for the reasons of record, this rejection of claims 9-11 is maintained.

24. **(Prior Rejection- Withdrawn)** Claim 12 was rejected under 35 U.S.C. 103(a) as being unpatentable over Bass, in view of the 1998 article, and the Spaete patent, and further in view of Barenkamp the 182 patent and Recombinant DNA. In view of the amendments to the claim, and the fact that the prior art does not teach or suggest the precise plasmid claimed, the rejection is withdrawn.

Conclusion

25. No claims are allowed.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
February 13, 2003

JAMES HOUSEL 2/23/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

JASEMINE C. CHAMBERS
DIRECTOR
TECHNOLOGY CENTER 1600